UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,698	12/05/2001	Victoria Pope	6395-61750	1330

24197 7590 06/17/2003

KLARQUIST SPARKMAN, LLP
121 SW SALMON STREET
SUITE 1600
PORTLAND, OR 97204

EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	8

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/009,698	Applicant(s) POPE ET AL.	
	Examiner Khatol S Shahnan-Shah	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' preliminary amendment A, received 12/05/2001, paper #3 is acknowledged. Claims 22-25 were added. Priority statement was added to page 1 of the specification.

2. Applicants' Information disclosure statement, received 12/05/2001, paper #3 is acknowledged the references have been considered by the examiner.

3. Currently claims 1-25 are pending and under consideration.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 12-21 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting anti-lipoidal antibodies that are generated upon possible infection by *Treponema pallidum*, does not reasonably provide enablement for detecting the presence of *Treponema pallidum* in a biological sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method for detecting the presence of *Treponema pallidum* in a human using a composition comprising synthetic cardiolipin and synthetic lecithin. The specification fails to describe the source of the synthetic cardiolipin and synthetic lecithin. Specification page 5, lines 10-25 recites poor specificity in non-treponemal tests due to false positive and false negative results when using these tests when patients suffers from other

medical conditions including mycoplasma infection, pneumonia, malaria, acute bacterial and viral infections and autoimmune diseases. In line 25 applicants emphasize on the use of alternative methods for confirmation, which is normally required. These tests are standard treponemal- based test such as microscopy or fluorescent treponemal antibody absorption (FTA-ABS). Claim 12 recites detecting the presence of *Treponema pallidum.* However, applicants' composition and method are also based on non-treponemal test such as VDRL. Example 5, pages 24-25 in table 6 shows the comparative analysis of synthetic VDRL antigen and natural VDRL antigen in biological false positive samples. The results of table 6 show no difference in regard to sensitivity or specificity between these tests and both test still require confirmation by a treponemal- based test. It is not clear from the specification if one skilled in art would have been convinced by using the claimed synthetic composition to rely on the positive result of this test and could have been concluded the presence of *Treponema pallidum* in the patient's sample without the use of alternative methods for confirmation which is normally required in diagnosis of syphilis.

Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the court of appeals in In re Wands, 8 USPQ 2d 1400 at 1404 (CAFC 1988).

These factors include 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, and 8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) insufficient

direction or guidance is presented in the specification with respect to detecting the presence of *Treponema pallidum* in a human 2) the nature of the invention involved the complex area of syphilis serology, 3) the state of the prior art shows the lack of good specificity in non-treponemal tests for detection of syphilis. Therefore, because of lack of guidance and lack of predictability in the art it is determined that it would require undue experimentation to make and use the invention commensurate in scope with these claims.

6. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a concentration of cardiolipin of approximately between 0.02 and 0.04 % in the claimed composition, does not reasonably provide enablement for the concentration of cardiolipin of approximately between 0.01 and 0.05 % in the claimed composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 16 recites a method of claim 12, wherein the concentration of cardiolipin in the composition is between approximately 0.01 and 0.05%. The specification is only enabled for a concentration of cardiolipin between approximately 0.02 and 0.04% by volume and more preferably 0.03% (see page 11). The instant specification invites the skilled artisan to experiment. The factors, which must be considered in determining undue experimentation, are set forth in In re Wands USPQ2d 14000. The factors include

1) quantity of experimentation necessary,
2) the amount of guidance presented,
3) the presence or absence of working examples,
4) the nature of the invention,

5) the state of the prior art,
6) the predictability of the art and the
7) breath of the claims.

With regard to factors one and two cited above the quantity of experimentation needed to determine the concentration of cardiolipin in this composition has not provided adequate guidance in the written description for accomplishing and determining such.

With regard to factors four and six, it is noted that there is a great deal of unpredictability in specificity and sensitivity of serological detection of syphilis. The instant specification fails to provide a specific methodological procedure for which the instant method can or is intended to be used for detecting the presence of *Treponema pallidum* in the biological sample and it fails to mention any specific significance of the % cardiolipin in the composition intended for the detection of *Treponema pallidum*. Therefore, it is determined that it would require undue experimentation to make and use the invention commensurate in scope with the claim.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 2- 8, 11, 13-14, 16-17 and 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "approximately" and "between approximately" in claims 3, 5- 8, 14, 16-17 and 22-25 are relative terms which render the claim indefinite. The terms are not defined by the

claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-8, 11 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Yabusaki, K. K. (US 4,738,932).

The claims are drawn to an antigen composition comprising synthetic cardiolipin, synthetic lecithin, cholesterol and ethanol.

Note: The subject matter of independent claims 1 and 22 relates to an antigen composition comprising synthetic cardiolipin and synthetic lecithin. Since the claims do not provide a more specific determination of said synthetic substances, they include any cardiolipin and lecithin having been produced artificially. Even natural cardiolipin and lechithin fall under the scope of the claims, since cardiolipin and lechithin can have been produced artificially with the same structure as the natural ones, i.e. no distinction of the products is possible. A compound is not rendered novel merely by the fact that is produced by means of a new process.

Yabusaki, K. K. discloses an antigen composition comprising synthetic cardiolipin, synthetic lecithin, cholesterol and ethanol (see claim 7). Yabusaki teaches a composition wherein the concentration of cardiolipin is 0.03 %, concentration of cholesterol is 0.9 %, and

concentration of lecithin is approximately 0.21 % (see claim 7, column 3, lines 10-25 and column 4, lines 61-65). The prior art anticipates the claimed invention.

Since the office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed composition and the composition of the prior art (i. e., that the composition of prior art does not possess the same material structure and functional characteristics of the claimed composition). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claims 1-8, 11 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Barner et al. (US 4,307,074). Prior art of record, applicants' 1449.

The claims are drawn to an antigen composition comprising synthetic cardiolipin, synthetic lecithin, cholesterol and ethanol.

Note: The subject matter of independent claims 1 and 22 relates to an antigen composition comprising synthetic cardiolipin and synthetic lecithin. Since the claims do not provide a more specific determination of said synthetic substances, they include any cardiolipin and lecithin having been produced artificially. Even natural cardiolipin and lechithin fall under the scope of the claims, since cardiolipin and lechithin can have been produced artificially with the same structure as the natural ones, i.e. no distinction of the products is possible. A compound is not rendered novel merely by the fact that is produced by means of a new process.

Barner et al. disclose an antigen composition comprising synthetic cardiolipin, synthetic lecithin, cholesterol and ethanol (see claims 1, 3-7 and example in column 4, line 25-35). Barner et al teach a composition wherein the concentration of cardiolipin is 0.02 %,

concentration of cholesterol is 0.9 %, and concentration of lecithin is approximately 0.12 % (see claim 6). The prior art anticipates the claimed invention.

Since the office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed composition and the composition of the prior art (i. e., that the composition of prior art does not possess the same material structure and functional characteristics of the claimed composition). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

12. Claims 1-2, 4 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Gokhale et al. (British Journal of Cancer, volume 74, no 1, pp. 43-48, 1996). Prior art of record, applicants' 1449.

The claims are drawn to composition comprising tetramyristoyl cardiolipin, lecithin, cholesterol and an alcohol.

Gokhale et al. teach a composition comprising tetramyristoyl cardiolipin, lecithin (phosphatidylcholine), cholesterol and an alcohol (see abstract and page 44 column 1, 3rd paragrph). The prior art anticipates the claimed invention.

13. Claims 12-17 and 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Yabusaki, K. K. (US 4,738,932).

The claims are drawn to a method for detecting the presence of *Trepanoma palidum* in a human comprising combining a biological sample from the human with a composition comprising synthetic cardiolipin and synthetic lecithin and detecting an immunocomplex formed between an antibody in the biological sample and the composition.

Yabusaki, K. K. discloses a method for detecting the presence of *Trepanoma palidum* in a human comprising combining a biological sample from the human with a composition comprising synthetic cardiolipin and synthetic lecithin and detecting an immunocomplex formed between an antibody in the biological sample and the composition (see claim 14 and column 2, lines 36-39). Yabusaki teaches that the immunocomplex is detected using agglutination test (see abstract). Yabusaki teaches a composition wherein the concentration of cardiolipin is 0.03 %, concentration of cholesterol is 0.9 %, and concentration of lecithin is approximately 0.21 % (see claim 7, column 3, lines 10-25 and column 4, lines 61-65). The prior art anticipates the claimed invention.

Since the office does not have the facilities for examining and comparing applicants' method with the method of the prior art, the burden is on the applicants to show a novel or unobvious difference between the claimed method and the method of the prior art (i. e., that the method of prior art does not possess the same material structure and functional characteristics of the claimed method). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

14. Claims 12-17 and 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Barner et al. (US 4,307,074).

The claims are drawn to a method for detecting the presence of *Trepanoma palidum* in a human comprising combining a biological sample from the human with a composition comprising synthetic cardiolipin and synthetic lecithin and detecting an immunocomplex formed between an antibody in the biological sample and the composition.

Barner et al. disclose a method for detecting the presence of *Trepanoma palidum*

in a human comprising combining a biological sample from the human with a composition comprising synthetic cardiolipin and synthetic lecithin and detecting an immunocomplex formed between an antibody in the biological sample and the composition (see column 1, lines 5 to 15 and claims 8-10). Barner et al. disclose that the immunocomplex is detected using flocculation test (see column 4, lines 5-10). Barner et al. disclose an antigen composition comprising synthetic cardiolipin, synthetic lecithin, cholesterol and ethanol (see claims 1, 3-7 and example in column 4, line 25-35). Barner et al teach a composition wherein the concentration of cardiolipin is 0.02 %, concentration of cholesterol is 0.9 %, and concentration of lecithin is approximately 0.12 % (see claim 6). The prior art anticipates the claimed invention.

Since the office does not have the facilities for examining and comparing applicants' method with the method of the prior art, the burden is on the applicants to show a novel or unobvious difference between the claimed method and the method of the prior art (i. e., that the method of prior art does not possess the same material structure and functional characteristics of the claimed method). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 1, 9, 10 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yabusaki, K. K. (US 4,738,932), and further in view of Avanti Polar Lipids product numbers 710332 and 850457.

The claims are drawn to an antigen composition comprising synthetic cardiolipin, synthetic lecithin, cholesterol and ethanol.

Yabusaki, K. K. discloses an antigen composition comprising synthetic cardiolipin, synthetic lecithin, cholesterol and ethanol (see claim 7). Yabusaki teaches a composition wherein the concentration of cardiolipin is 0.03 %, concentration of cholesterol is 0.9 %, and concentration of lecithin is approximately 0.21 % (see claim 7, column 3, lines 10-25 and column 4, lines 61-65). Yabusaki does not teach tetramyristoyl cardiolpin and 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine. However, these products have been known in the art and are commercially available from Avanti Polar Lipids Inc. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the commercially available pure synthetic cardiolipin and lecithin powders having product numbers 710332 and 850457 to obtain the claimed composition.

17. Claims 12, 18, 19 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yabusaki, K. K. (US 4,738,932), and further in view of Avanti Polar Lipids product numbers 710332 and 850457.

The claims are drawn to a method for detecting the presence of *Trepanoma palidum*

in a human comprising combining a biological sample from the human with a composition comprising synthetic cardiolipin and synthetic lecithin and detecting an immunocomplex formed between an antibody in the biological sample and the composition.

Yabusaki, K. K. discloses a method for detecting the presence of *Trepanoma palidum* in a human comprising combining a biological sample from the human with a composition comprising synthetic cardiolipin and synthetic lecithin and detecting an immunocomplex formed between an antibody in the biological sample and the composition (see claim 14 and column 2, lines 36-39). Yabusaki teaches that the immunocomplex is detected using agglutination test (see abstract). Yabusaki teaches a composition wherein the concentration of cardiolipin is 0.03 %, concentration of cholesterol is 0.9 %, and concentration of lecithin is approximately 0.21 % (see claim 7, column 3, lines 10-25 and column 4, lines 61-65). Yabusaki does not teach tetramyristoyl cardiolpin and 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine. However, these products have been known in the art and are commercially available from Avanti Polar Lipids Inc. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the commercially available pure synthetic cardiolipin and lecithin powders having product numbers 710332 and 850457 to obtain the claimed method.

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Oota et al. JP 10239315 published 9/11/1998.

JP 49046051 B published 12/7/1974.

JP 05312808 A published 11/26/1993.

Glbets et al. SU 629927 A published 10/5/1978.

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

June 12, 2003

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER